Federal Research on the Biological and Health Effects of Ionizing Radiation

Committee on Federal Research on the Biological and Health Effects of Ionizing Radiation
Division of Medical Sciences
Assembly of Life Sciences
National Research Council

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Preface

Toward the end of 1979, the National Academy of Sciences (NAS) was asked by the Director of the National Institutes of Health (NIH) to review and evaluate the scope and quality of research on the biological and health effects of ionizing radiation supported or conducted by agencies of the federal government. This request was made in response to legislation (PL 95-622, as amplified by supporting statements in the *Congressional Record* on October 14, 1978) requesting the Secretary of the Department of Health, Education, and Welfare (now the Department of Health and Human Services, DHHS) to develop a comprehensive strategy for research in this field. The legislation mandated that the strategy reflect not only the needs of agencies with obligations to develop new knowledge but also the needs of agencies with responsibilities to protect the public health.

In response to the NIH Director's request, the Committee on Federal Research on Biological and Health Effects of Ionizing Radiation (FREIR) was established within the Division of Medical Sciences, Assembly of Life Sciences, National Research Council The committee's charge included the following·

- a brief review of the state of knowledge on the biological and health effects of ionizing radiation (Chapters 4, 5),
- a review and evaluation of current research programs in this field (Chapter 9),

• an analysis of the relationship of the research supported or conducted by the several federal agencies to their goals and mission (Chapter 10),

• a critical evaluation of a government-wide agenda for future research into the biological effects of ionizing radiation, which i being developed by an Interagency Research Committee (IRC) (an interim draft of the research agenda was reviewed by the committee and its critique was delivered to the Director, NIH, for use by the IRC), and

• the identification of scientific studies that need special emphasis to improve the responsiveness of federal agencies to the problem of public health and safety created by ionizing radiation (Chapter 4-8)

The FREIR Committee's review and evaluation of current research involved not only an assessment of the relevant research program themselves but also an evaluation of the management practices used by the federal government to support these programs. The committee examined the scope and quality of the research programs as well a the quality of the control mechanisms built into the programs, e g selection and review processes, planning and execution of research and coordination among scientists and decisionmakers

ORGANIZATION OF THE STUDY

Approximately 900 research projects relating to the biological an health effects of ionizing radiation were identified by 15 federal agencies supporting research in this field This information was furthe corroborated by questionnaires completed by the principal investigators and by committee and consultant reviews of a representativ sample of projects

To facilitate the review process, the committee classified the research according to main objective and divided the studies into th following seven categories

• radiation sources and dosimetry,
• medical applications of ionizing radiation and radionuclides,
• control of occupational exposure to ionizing radiation,
• study of transport mechanisms and the effects of radiation an radionuclides on ecological and environmental systems,
• epidemiologic studies of the effects of ionizing radiation on humans,

- laboratory studies of the effects of ionizing radiation on animals, plants, lower forms, cells in tissue culture, and biological substrates, and
- measurements of dose-effect relationships, including the development of models for assessing risk.

No investigations relating to the management of radiation research were identified.

The committee was divided into five subcommittees, each with a specific assignment:

- *Subcommittee I—Overview* coordinated the work of the several subcommittees and blended their findings into this report.
- *Subcommittee II—Medical and Environmental Radiation* examined research on radiation instrumentation, dosimetry, control of occupational radiation exposure, the effects of environmental radiation, and the applications of ionizing radiation in medical diagnosis and therapy.
- *Subcommittee III—Epidemiology* reviewed research on the effects of ionizing radiation in humans.
- *Subcommittee IV—Nonhuman Radiation Effects* examined research on animals, plants, lower forms, cells in tissue culture, and biological substrates.
- *Subcommittee V—Management* studied the management processes used by the several federal agencies supporting and conducting radiation research programs.

Committee Procedure

The review of the research was accomplished in the following manner. Approximately 350 studies were identified as residing within the scope of Subcommittee II, 150 studies within Subcommittee III, and 400 studies within Subcommittee IV. The committee considered all research programs and then selected approximately 150 studies for in-depth, on-site reviews. These studies represented various categories of research that were conducted either intramurally or extramurally. Another 250 were selected for reviews based on submitted written and published information, which was assessed by reviewers and discussed by the subcommittees. All reviews were conducted by committee members and consultants from relevant scientific fields (see list on pp. iii-ix) who had been identified by the committee. In each case, the agency supporting the research, the institution in

which the research was conducted, and the project's principal in vestigator were contacted by staff of the Division of Medical Sciences They were informed in detail about the purposes of the reviews and were asked to supply background material, such as grant proposals recent progress reports, and publications The reviewers were aske to prepare reports describing each project, its aims, and procedures to provide an analysis of the progress, strengths, and weaknesse of the research, and to comment on the significance of researc results. The reviewers who conducted the site visits were asked t describe the relationship of each project to related work conducte at other institutions, to note the special resources available to th research team, and to review the mechanisms for reporting researc results and for accounting to the supporting agency

The reports prepared by the reviewers were circulated to the othe members of the review teams for additional comment Meetings wei then held by each subcommittee and its consultants to study th reviewers' reports and to discuss their general conclusions. Each (the several subcommittees then prepared an analysis of each of th research fields under its purview with attention to the followin items

- generic objectives of the projects reviewed,
- quality of the research,
- significance of the research;
- adequacy of the research,
- utilization of the research, and
- conclusions and recommendations of the subcommittee

Other sources of information were also used by the subcommittee For example, the Subcommittee on Management conducted appro imately 60 interviews with present and past directors and manage of federal research programs, congressional staff members, and rej resentatives of concerned environmental and scientific groups ar unions The interviews covered such matters as agency program research utilization, relationships among research programs, and oth factors influencing program management. A letter published in tl November 16, 1979, issue of *Science* magazine requested commen from members of the scientific community concerning goals that future research agenda should meet. Approximately 30 letters we received and evaluated. Comments were also collected at an ope meeting held in Washington, D C., on September 15, 1980 Tl meeting was attended by members of the public as well as by re

resentatives of interested environmental, consumer, industrial, and scientific organizations.

The FREIR Committee also conducted two workshops under the auspices of subcommittees II and IV. These workshops were designed to review current scientific knowledge with respect to the field of radiation biology, the uses of ionizing radiation in medicine, and the control of environmental contamination from radionuclides.

During the course of the FREIR Committee's work, there was much correspondence with federal agencies to determine their methods of identifying research needs, establishing research goals and priorities, evaluating and funding research proposals, reviewing the progress of supported and conducted research, and utilizing research results. The agencies and their representatives were most cooperative. They provided the committee with detailed information that is especially useful as a basis for understanding how the federal agencies perceive their goals and discharge their obligations.

The NIH provided the FREIR Committee with working papers containing extensive information, which served as the background for a public meeting held by NIH to discuss the strategies that might be followed in the development of federally sponsored research in radiation biology. The papers included reviews of current knowledge, identified major issues in each field of research, and outlined the kinds of information that should be developed to overcome deficiencies and uncertainties in the body of scientific knowledge on the biological and human health effects of ionizing radiation.

Seven appendixes have been prepared to supplement the information contained in this report. These have been published in a separate volume, which is also available from the National Academy Press. Appendix A describes the methodology used in this study and lists the projects identified by the committee. Appendixes B, C, and D complement discussions in the text of the main report by providing a more detailed and technical description of the committee's findings in the following areas: epidemiologic studies and other studies of the effects of ionizing radiation in humans, major sources of environmental and medical radiation, and external and internal radiation in animals. Appendix E explains the committee's procedure for exploring management issues affecting the conduct of ionizing radiation research by federal agencies and lists the individuals interviewed in the pursuit of this information. The letter published in *Science* requesting suggestions pertaining to future research on the effects of ionizing radiation appears in Appendix F along with copies of the replies that were received. Appendix G describes the com-

mittee's procedure for reviewing research management practices o the federal agencies and contains letters from the agencies describing their activities in the area of research of interest to the committee.

The committee wishes to thank publicly the many scientific consultants who contributed so much to the development of this report. It is also grateful to the many public officials and private citizens who responded thoughtfully and thoroughly to the committee's requests for information, opinion, and guidance. It particularly wishes to thank the scientific investigators who gave so generously of their time and thought. The degree of cooperation obtained from all those who were encumbered with significant demands upon their time and effort bespeaks the extraordinary interest that everyone displayed in seeking to develop a comprehensive and useful document.

It wishes to single out for special thanks Dr. Donald S. Fredrickson, Director of the NIH, and Dr. Charles U. Lowe, Acting Associate Director, Medical Applications of Research, NIH, without whose help and cooperation this study could not have been completed.

The committee is grateful to the staff of the National Research Council, in particular to Dr. Daniel L. Weiss for his untiring assistance in coordinating the work of the committee, to Dr. Eli Salmon, Senior Staff Officer of the committee, and his assistants, Ms. Elizabeth Harvey and Dr. Dwain Parrack, and to Ms. Frances M. Peter, Staff Editor of the report.

It is our hope that the information provided in this report will be useful to the Congress, the federal establishment, and the scientific community in the planning and management of federally supported research on the biological effects of ionizing radiation in the years ahead.

RUSSELL H. MORGAN
Chairman
Committee on Federal Research on
Biological and Health Effects of
Ionizing Radiation

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Executive Summary

During the past half century, federally supported research has provided a vast body of knowledge on the biological effects of ionizing radiation. Probably more is currently known about the health risks of ionizing radiation than about any other potentially hazardous agent. As a consequence, there exists a body of scientific information that permits federal authorities to formulate a reasonably conservative and effective system of radiation protection standards and to delineate comprehensive regulatory policies

As in all scientific disciplines, much remains to be learned. It is therefore important that future research be carefully planned and effectively carried out within the limits of available resources

Current research constitutes but a small increment of a much larger investigative effort that had its beginnings several decades ago. The committee finds that its quality is generally good With few exceptions, this research appears to be well conceived and carefully pursued by competent scientists This is due in no small part to the procedures used by federal agencies to determine that the research objectives and experimental designs of work proposed by their contractors and grantees are appropriate and that the work is carefully and diligently performed. These procedures differ from agency to agency Some agencies, such as the National Institutes of Health (NIH), use a process of external peer review in which research proposals of a given discipline are reviewed by scientists of similar disciplines In other agencies, such as the Department of Defense

(DOD), the Department of Energy (DOE), and others, research prc posals may be evaluated by agency staff members knowledgeable ı the proposal's subject matter and by external peer reviewers. Vari ations and combinations of these procedures are also used.

Each of the systems has its advantages and disadvantages. How ever, with the increasing number of federal agencies having an in terest in radiation research, the committee believes that there is meri in the adoption of a comparable system of evaluation and review with a more standardized protocol of how to report results so tha they can be combined from several studies sponsored by the differen agencies. Of the various systems in use, external peer review seems to be the most objective and provides a means of introducing a broac range of expert scientific guidance to the evaluation and review proc esses

Recommendation 1. The committee recommends that federally supportec research on the biological effects of ionizing radiation be evaluated withir systems of external peer review that are roughly comparable to each other

The following paragraphs contain the committee's conclusions and recommendations for specific fields of research

Radiation Dosimetry

In radiation dosimetry, there can be no question about the usefulness of continuing research to improve dosimetric instrumentation Radiation standards and policies are dependent upon the availability of a broad range of appropriate instrumentation for use by public officials and others involved in the application of ionizing radiation The committee notes that the quality of dosimetric research in recent years has been exceptional

From its review of current research, the committee concludes that dosimetric capabilities are reasonably adequate for electromagnetic radiation and charged particles but that dosimetry of neutrons and of mixed radiations requires further development. It also notes that *in vivo* measurements to determine doses from nonuniform distributions of radionuclides deposited within the body should also be improved. Finally, the assessment of radionuclide doses to particular organs, and to specific cells within organs, is in continuing need of further study. Studies of radionuclide uptake, deposition, metabolism, and elimination play an important role in health protection and should therefore be encouraged Priority should be given to radionuclides to which large populations of humans are exposed

Recommendation 2 The committee recommends that emphasis be placed

upon dosimetric research for neutrons and mixed radiations Added emphasis should also be placed on the development of dosimetric instrumentation to be used in measurements of nonuniform field distributions of radionuclides Particular attention should be directed toward measurements of doses to organs and tissues and to specific cells within these organs and tissues

EPIDEMIOLOGIC RESEARCH

In the past, much has been learned regarding the health risks of ionizing radiation from epidemiologic studies of such population groups as the survivors of the Japanese bombings, the uranium mine workers, and several groups of patients in whom x-rays have been used diagnostically and therapeutically Epidemiologic studies by their very nature extend over long periods. Thus, many of them are still in progress These studies should be continued with periodic peer review until they have reached their logical conclusions. This may require the protraction of the Japanese studies at least until the end of the life spans of nearly all the irradiated persons and may justify study of subsequent generations assuming that observational techniques now available, or that may be devised, promise to yield new worthwhile information on radiation risks

Future epidemiologic studies should be undertaken only with great care From time to time, there will undoubtedly be populations in which exposures to ionizing radiation have occurred and which for various reasons may seem attractive for intensive study Seldom, however, will these populations be sufficiently large, nor will their radiation doses be well documented and of adequate size to yield statistically significant data on dose-effects relationships and radiation risk

The committee notes that federal agencies supporting epidemiologic research in recent years have tended to establish their priorities in a manner that is more haphazard than orderly As a consequence, excessive effort has been directed toward epidemiologic studies of populations exposed to low-dose radiation. Because the results of such studies are likely to be unrewarding, the committee urges that the federal agencies involved in epidemiologic research undertake a restructuring of priorities

Recommendation 3. The committee recommends that currently supported, large-scale epidemiologic studies on the health effects of ionizing radiation be continued with periodic peer review until they have reached their logical conclusions. Meanwhile, federal agencies supporting epidemiologic research in this field should reexamine their priorities and confine future scientific

research to areas that are likely to yield statistically reliable data. The committee recognizes that social and political processes may require responses in the form of surveys and epidemiologic studies even when such efforts are predictably unrewarding scientifically In such cases, a clear distinction should be made between these studies and those that are scientifically justifiable.

RESEARCH ON ANIMALS, LOWER LIFE FORMS, PLANTS, CELLS IN TISSUE CULTURE, AND BIOLOGICAL SUBSTRATES

Because experience with the effects of ionizing radiation in humans, exposed either accidentally or by design, is necessarily limited, research on animals serving as surrogates for humans and research on animals, lower life forms, cells in tissue culture, and biological substrates to gain an understanding of fundamental radiobiological principles currently constitute the principal avenue of investigation to increase knowledge of the risks to health from exposure to ionizing radiation Indeed, this is a useful approach to determining dose-response relationships in humans for lifetime dosage levels below 50 rem

The major health risks following exposure to ionizing radiation include the development of cancer several years later and the development of genetic aberrations or mutations in future generations of exposed individuals Much can be learned regarding these risks from radiobiological research. However, the fact that such observations are not made in humans raises important questions regarding their applicability in determinations of human risk. Such questions may be expected to disappear only when future research leads to an understanding of the basic principles involved—principles that apply to all living species

Recommendation 4. The committee recommends that future studies in the field of radiation biology place increased emphasis on an understanding of the mechanisms of radiation carcinogenesis This is particularly important with respect to carcinogenesis following low doses of low linear energy transfer (LET) radiation This research should involve cellular and molecular experiments combined with selected studies on irradiated animals and appropriate observations of irradiated human populations The committee encourages the design and conduct of experiments that test current concepts in models of carcinogenesis in general and radiation carcinogenesis in particular

The risks of genetic effects from exposure to ionizing radiation have been quantified, to the limits of present knowledge, in the "BEIR III Report" (National Academy of Sciences, 1980). Because of the uncertainty surrounding the nature of the various forms of ge-

netic damage, and their biological consequences, the estimates of risk to humans are imprecise Consequently, studies in radiation genetics addressing these uncertainties must continue, particularly at the molecular and cellular levels. Furthermore, because reproductive processes such as meiosis and gametogenesis play a large role in the transmission of genetic damage, experimental work is still needed on whole organisms Additionally, studies will also be required on single cells from animals and plants and on single-celled organisms, especially at very low doses

Recommendation 5· The committee recommends that future research on radiation genetics place increasing emphasis on resolving the uncertainties surrounding the nature of genetic damage and its biological consequences whether or not radiation is used as a probe of the system Such research should be directed toward observations not only on single cells from animals and plants but also of whole organisms

In addition to the need for greater understanding of the basic mechanisms involved in the response of biological systems to ionizing radiation, there is also need for further observations on the responses of whole animals Such research should be directed toward evaluating the effects of radiation on such subpopulations as developing fetuses, newborn animals, and organisms with special properties influencing their sensitivity to radiation Physiological and metabolic processes that determine dose distributions from both internal and external radiation sources should be included in these studies

Recommendation 6· The committee recommends the continuance of research on radiation effects on whole animals, especially studies evaluating these effects in appropriate subpopulations and the physiological and metabolic processes that determine dose distributions in both time and space from internal and external radiation sources

The raw data generated over the last 35 yr on the delayed effects, both internal and external, of ionizing radiation in animals are the product of an enormous public investment in scientific effort, animals, and money It has often been recommended in the past that an adequately funded central national archive be established to accommodate this material and make it accessible for continued use Since many senior investigators in the older projects are approaching retirement age or are being diverted to other work, it is important that their data be retained so that they may be available for use by future scientists At a time when new studies are few and must be planned with special care, the existence and accessibility of such a data bank would be of great value.

Recommendation 7: The committee urges the creation of an adequatel funded central national archive to accommodate the vast amount of raw dat on the late radiation effects in animals that have accumulated over the las 35 yr in order to make them accessible for future use

Environmental Exposure and Radionuclide Transport

In recent years, research directed toward an understanding of th environmental transport of radionuclides has been limited in scope Following the discontinuation of nuclear weapons testing in the at mosphere, interest in this field appears to have diminished Althoug environmental research in the past appears to have provided a adequate basis for the formulation of radiation protection standard and regulatory policies with respect to radionuclide contaminatio of the environment under normal conditions, there is some questio regarding the adequacy of current knowledge regarding accidental large-scale releases of radionuclides Because evaluation of recover from damage to ecological systems from radionuclide contaminatio requires months and years of observation, it is important that long term commitments be made to research programs in this field More over, multifactorial experimental work is necessary to identify th additive and synergistic effects in which radionuclide releases ar accompanied by other stress factors There is also a need to develo better models to describe the relationships among radiation sourc factors, radionuclide dispersal, various biotic processes, and effects Predictions of these relationships from current models present man uncertainties, largely due to a lack of field validations of these model under various environmental conditions

Recommendation 8 The committee recommends that long-term, broadl focused research programs be undertaken to increase understanding of th complex transport systems used by radionuclides in a contaminated environ ment Supportive research on dietary pathways is especially important. Ad equate support should also be given to the continuing development and val idation of models by which radionuclide levels within the ecological systen may be predicted following radionuclide contamination of the environment

Occupational Exposure

Levels of occupational exposure to radiation are currently well unde the limits now considered to be acceptable In occupational group surveyed by DOE and the Nuclear Regulatory Commission (NRC) the average dose per worker has remained essentially constant. Thi

indicates general adherence to present regulations with respect to radiation exposure limits and suggests that risks from occupational exposure are quite low Although this may be true in general, an exception may be found in certain mining operations where radon levels are difficult to control and many uncertainties exist in regard to the dosage received *More importantly, critical epidemiologic studies must be pursued in such areas as uranium mining to relate dosage and time of exposure to the development of lung cancer and the significance of other carcinogens such as cigarette smoke, asbestos, and possibly other cocarcinogens* Another area of insufficient research is chelation therapy, which can improve the removal of radionuclides from internally contaminated workers

In recent years, efforts to improve dose measurement or to reduce dose for workers in the medical, mining, and nuclear industries have been limited

Recommendation 9 The committee therefore finds that practical methods to improve occupational dosimetry and to reduce radiation exposure require greater emphasis, and urges attention to vulnerable occupational groups, especially in the mining industries.

Reduction of Risks from Radiation Therapy

During the past two decades, there has been relatively good support for research designed to improve radiation therapy to treat cancer patients In such treatment, only a portion of the radiation administered to patients is effectively concentrated on the cancerous lesion. Healthy tissues are also irradiated, thereby being subject to potential damage Consequently, it has been a main concern of the committee to review research directed toward improving the ratio of the tumor radiation dose to the total patient dose In general, this research has been of good quality, and the committee recommends its continued support

Radiation-induced carcinogenesis in radiation therapy patients should be evaluated and the treatment modified to reduce the incidence of such carcinogenesis These evaluations should be both retrospective and prospective and should include not only factors in radiation treatment but also the influence of chemotherapy in combined programs with respect to the initial appearance of cancer

Recommendation 10· In the field of radiation therapy, research should be directed toward the understanding of radiation-induced carcinogenesis and the further improvement of the tumor.patient dose ratio

Reduction of Risks From Diagnostic Uses of Radiation

The diagnostic use of radiation in medical practice constitutes the largest source of ionizing radiation to which humans are exposed in the United States (excluding therapeutic radiation, which is administered to a very limited number of people). Because such use of radiation has unmistakable medical benefit, it is important that efforts be made to devise technologies in which benefit is enhanced and risk diminished. In the past, support for such research has been relatively small. To ensure that the best and most cost-effective radiological technologies for dose reduction and improved diagnoses are available to the public, the level of such support should be increased. More adequate funding commensurate with the increase in expenditures for radiological equipment and procedures made by the public and private sectors may be expected to improve the quality and productivity of research by enabling successful teams to continue their work and by raising the probability that worthwhile research proposals will be funded

Recommendation 11. The committee recommends that special attention be directed toward the development of medical technologies to increase the quantity of diagnostic information derived from these technologies while maintaining or reducing radiation dose Because the use of radiation in medical practice constitutes a large source of ionizing radiation to which humans are exposed, the committee also recommends the establishment of a focus for management, coordination, and funding of research programs in the medical radiological sciences

Risk Perception

In addition to scientific information, there are social, economic, and political factors that influence the setting of radiation standards and the development of regulatory programs Among these is the public's attitude toward radiation risk The public appears to accept the radiation risks associated with exposure to natural background and, with some concern, those due to medical sources The risks associated with facilities of the nuclear industry, especially those for generating nuclear power, have raised higher levels of concern After more than two decades of experience with such facilities in many countries and with a number of system failures including that at Three Mile Island, major segments of the public remain skeptical of their safety

The processes of selection of acceptable and unacceptable risks by

e public are complex and have a substantial bearing on energy licy within the legislative and executive branches of the govern-ent. Although the committee makes no specific recommendations this area, it believes that research conducted to gain a better iderstanding of the bases upon which risk judgments are made n be useful

ANPOWER

wide range of disciplines is required for research on the biological d health effects of radiation These include radiation biology, ra-ation physics, epidemiology, biostatistics, management science, netics, clinical medicine, and pathology Manpower requirements ve not been systematically studied by this committee with respect radiation research Moreover, the broad manpower needs of the quired disciplines are not known at this time. However, it is noted at limiting manpower situations may exist in a number of disci-nes, for example, in the fields of epidemiology, radiation biology, d ecology.

Recommendation 12. The committee recommends that a study of manpower eds with respect to research on the health and biological effects of radiation undertaken. The study should be designed to provide information that uld clarify the nature and effects of the manpower limitations and suggest ecific and interdisciplinary training programs in those areas in which man-wer needs are not being met.

ESEARCH MANAGEMENT

iring the past 10 yr, considerable fragmentation has occurred within e administration of federally supported research on the biological ects of ionizing radiation Many agencies are now involved in these ograms, whereas during the 1950's and early 1960's the great ma-ity of such research was supported by the then-existing Atomic iergy Commission.

This fragmentation does not appear to have been detrimental to e quality or conduct of the research. On the contrary, it may have en beneficial by providing multiple focal points for different in-ests and emphases and greater opportunities for funding a wide riety of research

Still, there is a need to coordinate research on the effects of ra-ation. Gaps in the information base must be identified Problems mmon to various agency interests require consideration Joint re-

sources should be allocated through consultative arrangements Se rious interagency review must be given to major undertakings, es pecially to the initiation of new epidemiologic studies The FREIF Committee also recognizes the need to coordinate the regulation o radiation sources

At present there are two separate committees whose function is to coordinate the development of federally sponsored radiation pro grams. These are the Interagency Radiation Research Committee (IRRC) and the Radiation Policy Committee (RPC) The committee proposes a consolidation of these two committees, thereby combining their functions

What seems to be needed now, after the major changes that have occurred during the past decade or so, is an opportunity for the several federal agencies that have been given responsibility for the administration of research on the biological effects of ionizing radiation to carry out their functions without organizational disruption and distraction. If this is done, the radiation research programs of the future will probably be as productive and distinguished as those of the past

Recommendation 13· Because of the overlapping functions and interdependent relationships of the IRRC and RPC, the committee recommends that they be combined

In the interests of long-range productivity and the attraction and retention of competent scientists in radiation-related research, attention should be given to the concept of stability and continuity of research programs This might be accomplished by more frequent awards of 5-yr contracts for both new and renewal projects that peer groups have judged to have a high probability of producing important results Longer funding cycles have the additional advantage of reducing the need for frequent peer reviews

Recommendation 14. The committee recommends that in the interests of long-range productivity of research, including that on the biological effects of ionizing radiation and their abatement, more emphasis be placed on the awarding of multiyear contracts and grants

REFERENCE

National Academy of Sciences 1980 The Effects on Populations of Exposure to Low Levels of Ionizing Radiation Report of the Committee on the Biological Effects of Ionizing Radiations National Academy of Sciences, Washington, D C 638 pp

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The Radiation Sciences—An Overview

Because the readers of this report may have widely different backgrounds, this chapter and Chapter 3, highlighting the basic principles and definitions of the radiation sciences, have been prepared to assist those not conversant with these subjects to gain a better understanding of the basis for the following chapters concerning the health risks associated with the uses of ionizing radiation and the biological research that is needed to improve risk assessment and abatement Those familiar with these matters should proceed directly to Chapter 4

THE MATERIAL UNIVERSE

The fundamental constituents of the universe in which we live are matter and energy, each of which can, under appropriate conditions, be transformed into the other Examples of matter include the things that we see and feel around us such as the land, the sea, the forests, the sun, and the planets. Examples of energy include electromagnetic radiation such as radio waves, infrared radiation, light, ultraviolet radiation, x-rays, and gamma rays, and the motions associated with matter.

The material world is extremely complex. It is composed of a great variety of physical, chemical, and biological forms Nevertheless, all of these forms are composed of a series of building blocks whose characteristics exhibit a disarming orderliness. To illustrate, consider

what happens when a pure substance, such as a crystal of table salt or sugar, is divided and redivided over and over again into smaller and smaller units. Ultimately, there comes a time when the crystals are no longer recognizable as parts of the substance. At this stage, the crystals of salt or sugar no longer exhibit *any* of the physical or chemical properties of salt or sugar.

The smallest particle into which a substance can be divided and still retain its characteristic properties is called a *molecule*, of which there are many, many kinds. Arranged in an almost endless variety of combinations and configurations, they comprise one of the basic species of building blocks that form the material universe.

If the process of division is carried further, the molecule is found to be composed of a series of even smaller particles, called *atoms*. Like molecules, atoms come in a variety of classes, the properties of each depending on a still smaller series of particles of which they are composed. The initial concepts of atomic structure were first postulated in 1913 by Niels Bohr. He pictured the atom as an infinitesimally small solar system, consisting of a heavy central core or *nucleus* having a positive electrical charge, and a number of light, orbiting particles called *electrons*, each carrying a negative electrical charge. Since that time, the Bohr model of the atom has undergone considerable revision as new knowledge has become available, however, the model is a useful concept for this discussion.

With the exception of the common form of the hydrogen nucleus, atomic nuclei are composed of two types of relatively heavy particles—the *proton*, with a mass of 1.673×10^{-24} grams (g), and the *neutron*, with a mass of 1.675×10^{-24} g. These masses are approximately 1,800 times greater than that of the electron. The proton carries a positive electrical charge that is equal but opposite in sign to the charge on an electron. The neutron has no electrical charge.

The amount of electrical charge carried on an electron is extremely small. It requires a flow of 6.2×10^{18} electrons per second to produce an electrical current of 1 ampere (A), which is approximately the amount of current flowing in a 100-watt (W) lamp that is connected to a conventional 110-volt (V) household power source.

In neutral atoms, the number of positive charges carried on the protons of an atomic nucleus is equal to the number of negative charges carried on the atom's orbital electrons. Because opposite electrical charges attract each other, the electrons are maintained in their orbits by a balance between the electrical forces of attraction toward the nucleus and the centrifugal forces associated with the motions of the electrons.

The chemical properties of an atom are governed by the number of protons (and electrical charges) within the atom's nucleus In nature, there are 92 species of atoms whose number of nuclear protons range systematically upward from hydrogen, which has a single proton, to uranium, which has 92 Each of these species is called an *element* In recent years, several elements of greater nuclear size and electrical charge have been produced artificially in nuclear reactors and by particle accelerators. Plutonium-239, with a nucleus of 94 protons and 145 neutrons, is an example of such an atom. The number of protons within the atomic nucleus of an element is called the element's *atomic number* As the atomic number increases, the ratio of neutrons to protons in atomic nuclei tends to become larger.

An element with a given atomic number may exist in several forms, depending upon the number of neutrons included in the atomic nuclei For example, hydrogen occurs in three forms· one has a single proton as its nucleus, a second (called deuterium) has a proton and a neutron as its nucleus, and a third (called tritium) has a proton and two neutrons The various forms of a particular element are called *isotopes* of that element All exhibit identical chemical properties, but have different atomic weights The various forms of all atomic species are generally referred to as *nuclides*

Many nuclides are unstable, undergoing spontaneous nuclear disintegration (*radioactive decay*) during which certain energetic particles and gamma rays are emitted Such nuclides are called *radionuclides*

Energy and Ionizing Radiation

The forms of energy of greatest interest in this report are the energies associated with certain charged particles (e.g , electrons and protons) and uncharged particles (e.g., neutrons and electromagnetic radiations)

The particles of electromagnetic radiations are called *photons*. The several forms of electromagnetic radiation (e.g , radio waves and light) differ from one another only with respect to the amount of energy associated with each photon For radio waves, the amount of this energy is extremely small As one proceeds through the spectrum from infrared radiation to light, ultraviolet radiation, and, ultimately, to x-rays and gamma rays, the amount of energy becomes progressively greater For instance, the energy associated with x-rays and gamma rays reaches levels so great that when these radiations fall upon and impart their energy to matter, orbital electrons are ejected from the material's atoms.

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The energies associated with charged and/or uncharged p
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is equal to 1.6 × 10 watt seconds (W-s). X-rays used in m
practice range upward in energy from approximately 10,000 e
to many million electron volts (MeV) per photon. The radia

emitted during radioactive decay also have energies extending over a wide range

Another type of nuclear disintegration requires mention here because it is a source of many man-made radioactive materials This is the process of *nuclear fission,* which occurs when certain heavy elements (e g , uranium-235) are bombarded with neutrons As a neutron enters and reacts with an atomic nucleus of such an element, the atom splits into two fragments The sum of the atomic numbers of the two fragments equals the atomic number of the parent atom Because the ratio of neutrons to protons in atomic nuclei increases with atomic number, several neutrons are left over when nuclear fission occurs and many are set free Some of these may be captured by other fissionable atoms, and the process is continued in a self-sustaining chain reaction until the number of neutrons and/or the availability of fissionable nuclei drop below critical levels

The fission fragments are usually radioactive, emitting beta particles and, often, gamma rays

Every fission is accompanied by the release of substantial amounts of energy (approximately 100 times more than that released during radioactive decay and many million times more than that released during such molecular processes as the burning of coal). Controlled nuclear fission has therefore taken on importance as a means of producing electrical power

Properties of Ionizing Radiation

Absorption

When ionizing radiation impinges upon matter, some or all of the energy associated with the radiation is transferred to the atoms of the impacted matter in a process called *absorption* When biological cells or tissues are irradiated, this process sets into motion a series of chemical reactions and biological changes of far-reaching importance

The physical absorption of energy from ionizing radiation results in two reactions *excitation* (the elevation of energy levels of orbital electrons without their removal from their parent atoms) and *ionization* (the actual ejection of orbital electrons) As previously stated, removal of an electron from a neutral atom creates a positive ion, whereas the capture of such an electron elsewhere produces a negative ion Hence, a pair of ions is formed in each ionization event.

An atom from which one or more orbital electrons have been ejected exhibits a positive electrical charge and is called a *positive ion* The ejected electrons may attach themselves to electrically neutral atoms nearby. These atoms then become negatively charged and are called *negative ions* Such a process is referred to as *ionization* Hence, electromagnetic radiation having sufficient photonic energy to cause ionization is called *ionizing radiation*

Energetic subatomic particles also have the capacity to ionize the matter with which they interact. Therefore, they too are ionizing radiation. Among these are the charged particles emitted during radioactive disintegration or decay

The production of ionizing radiation involves processes in which forces both within and external to atomic nuclei play a key role. To illustrate, x-rays may be created when energetic electrons interact with the forces prevailing in the extranuclear regions of the atoms of a material on which they impinge This occurs in x-ray tubes The radiations emitted during radioactive decay are generated when forces within the nuclei of unstable atoms cause the nuclei to undergo rearrangement with the splitting-off of some of their components

Naturally occurring radionuclides may emit three types of radiation. One consists of energetic, negatively charged electrons, which are called *beta particles* to distinguish them from energetic electrons produced in other processes. The second consists of helium nuclei, which are composed of two protons and two neutrons These energetic particles are called *alpha particles* The third is electromagnetic radiation Such radiation has been given the special name *gamma radiation* to distinguish it from electromagnetic radiation originating outside the nucleus (x-rays) In each disintegration, one charged particle only is emitted. Gamma radiation is also emitted if the energetics of the particular disintegration scheme requires it Man-made radionuclides may also include a variety of disintegration schemes in which the emitted charged particle is a fourth type of radiation consisting of *positrons* These particles have the same rest mass as that of electrons but carry a positive electrical charge.

The energies associated with charged and/or uncharged particles of ionizing radiation are customarily measured in units called *electron volts* (eV) An electron volt is the quantity of energy imparted to an electron when it is moved through an electrical potential of 1 V. It is equal to $1\ 6 \times 10^{-19}$ watt-seconds (W-s) X-rays used in medical practice range upward in energy from approximately 10,000 eV (10 keV) to many million electron volts (MeV) per photon. The radiations

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PROPERTIES OF IONIZING RADIATION

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On the average, the production of each ion pair and a few excitati events require the absorption of approximately 34 eV of energy common, noncrystalline materials (e g , air, water, tissues, etc).

Most electrons ejected from the atoms of an irradiated volume matter are sufficiently energetic to induce ionization themselves I deed, most ion pairs arise secondarily in this manner. Only a fe are produced directly by interactions involving the incident phot radiation itself in so-called primary ionizing events. Charged particl ionize and excite directly.

In tissues, chemical changes may occur in molecules containi both excited and ionized atoms This activity may be accompani by the formation of highly reactive intermediates that induce chang in nearby molecules Nearly all of these reactions take place with a small fraction of a second In contrast, the biological consequenc sometimes require many years to manifest themselves

When particles of ionizing radiation are absorbed into matter, pr mary ionizing events are distributed along the radiation's trajector For some types of radiation, e g , helium nuclei and protons, spacir of these events is relatively close For others, such as x-rays an gamma rays, the events are spaced relatively far apart The line rate at which radiant energy is transferred or imparted to matt along a particle's pathway or, stated more simply, the *linear energ transfer (LET)* of radiation, is clearly greater for some types of radiatio than for others. The LET of radiation has a strong influence on th extent of the damage produced in biological tissues the higher th LET, the greater the damage

ALPHA PARTICLES

Alpha particles constitute an example of high-LET radiation A typic alpha particle, whose energy is 5.5 million eV (5.5 MeV), has a rang of only 40 micrometers (μm) in soft tissues (approximately four ce diameters) Moreover, approximately 40,000 ion pairs are produce by such an alpha particle as it traverses a typical cell Hence, th ionization resulting from the absorption of an alpha particle is con centrated in an extremely small volume and, when it occurs withi a cell, may cause severe disorganization of the cell's constituent (such as the strands of genetic material)

NEUTRONS

Fast neutrons, whose energies range from 10,000 eV (10 keV) to 1 MeV, lose their energy through collision with atomic nuclei Th

recoiling atoms, stripped of some of their orbital electrons, create dense tracts of ionization somewhat similar to those of alpha particles In soft tissues containing large numbers of hydrogen atoms, the recoiling nuclei from neutrons are mainly protons, which can cause severe biological damage

After a neutron has lost nearly all of its kinetic energy in repeated collisions, it is called a thermal neutron Typically, the thermal neutron is captured by the nucleus of an atom With this capture, a gamma ray is often emitted

Beta Particles

Beta particles (the high-speed electrons emitted from disintegrating atomic nuclei) have a range in soft tissues considerably greater than those of alpha particles of similar energy. For example, a typical beta particle, having an energy of 2 MeV, has a range of approximately 1 cm (about 1,000 cell diameters) Such a particle produces approximately 60 ion pairs while traversing a typical cell Whereas alpha particles cause intense ionization of a few cells, beta particles typically cause relatively sparse ionization within many cells. This distinction is particularly important if the target material of the cell is concentrated in its nucleus However, as beta particles and all other charged particles slow down, they produce increasing ion densities, reaching a maximum shortly before the ends of their paths Hence, low-energy electrons and other charged particles cause the formation of greater numbers of ion pairs per unit length of pathway near the end of their range than they do when they have greater energy.

Electromagnetic Radiation

The absorption of electromagnetic radiation (x-rays and gamma rays) may involve one or more of the following physical processes photoelectric absorption, Compton scattering, and pair production

During photoelectric absorption, the energy of an x-ray or gamma ray photon is imparted to one of the orbital electrons of an atom The electron is instantly ejected with an energy equal to the difference between the energy of the photon and that required to set the electron free This is the dominant absorption process for photons with energies below 50 keV Photoelectric absorption increases dramatically as the absorber's atomic number increases This is the principal reason why the absorption of diagnostic x-rays is substantially greater in bone because of its high calcium and phosphorus content than in

soft tissues, which are composed primarily of atoms with much atomic numbers

In Compton scattering, x-rays and gamma rays are deflecte free electrons or by orbital electrons of atoms, giving a part of energy to these electrons, which in turn recoil from the point of interaction The scattered radiation is thereby reduced in energ not eliminated during such encounters The photons that undergone Compton scattering proceed onward to be rescatter absorbed elsewhere. Compton scattering is roughly proportior the density and thickness of the absorbing material. It is aff little by the material's atomic number Hence, energetic gamma from cobalt-60 (1.17 and 1.33 MeV) and cesium-137 (0 66 MeV particularly useful in sparing bone from excessive damage d the therapeutic irradiation of tumors in nearby soft tissues.

In electron-positron pair production, the energy of an x-ra gamma ray photon is converted into an electron-positron pair sum of the energies of the electron and positron is equal t energy of the x-ray or gamma ray photon less the energy equiva of the rest masses of the electron and positron After slowing d the positron combines with a free electron that may be ava nearby Upon combination, the electron and positron are annihi with the production of two 0.51 MeV photons, emitted in direc nearly opposite to each other (back-to-back). Pair production o only near atomic nuclei and when the x-ray or gamma ray pł has an energy equal to or greater than 1 02 MeV, which is the er equivalance of the sum of the masses of the annihilated electror positron This mode of absorption increases slowly as photon er rises above the 1 02-MeV critical energy level

In each of the three primary modes of absorption of electro netic radiation, the energetic electrons accelerated as a consequ of absorption produce relatively sparse ionization and excitation their pathways in a manner similar to that produced by beta part X-rays, gamma rays, and beta particles are therefore classifie low-LET radiations

RADIONUCLIDES

Radionuclides comprise one of the major sources of ionizing r tion. Each radionuclide has a unique set of physical properties- types and energies of the radiations emitted and the rate of c (usually described by the radionuclide's physical half-life). More each radionuclide is an isotope of a chemical element and ext

the element's chemical properties, among them the ability to be oxidized or reduced, to form compounds and radical complexes, and to react with water (hydrolysis) Hence, the chemical properties of a radionuclide determine how it will react with other chemicals in the environment and in the tissues of plants, animals, and humans. In the environment, the chemical properties of a radionuclide also determine whether it will be associated with soil constituents or waters and whether it will be available for uptake by plants and/or animals (freshwater, marine, or terrestrial organisms) and eventually ingested by humans The chemical properties of an ingested radionuclide determine its ability to penetrate transport systems within the body, the efficiency of its absorption from the point of entry (i.e , the respiratory system, the gastrointestinal system, and/or the skin), its reactions with body fluids and cell constituents, its site or sites of localization within the body, and the manner and rate of its elimination from the body

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Radiation Quantities and Units

[illegible] their existence, humans have been exp[illegible] from natural sources. Some of the most in[illegible] rays and radiation emanating from r[illegible] from the earth, which often find their way int[illegible] construction materials.

[illegible] a useful tool of mankind had its begin[illegible] rays by Roentgen in 1895. Immediatel[illegible] of this discovery, there was a bur[illegible] before equalled. In medicine, the pote[illegible] at once, and before the turn of the cen[illegible] in active clinical use in every corner o[illegible] The excitement created by Roentgen's fin[illegible] by Becquerel's discovery of radioactivity [illegible] polonium and radium in 1898 by the Cur[illegible] of ionizing radiation were unknown. [illegible] x-ray "burns" began to appear in the me[illegible] the first physicians to use x-rays took [illegible] themselves from exposure to this new [illegible] of these pioneers fluoroscoped their hands [illegible] apparatus before their first patients were exami[illegible] that such a practice might be unwise. B[illegible] these physicians became inflamed and under[illegible] often degenerated into cancer of the skin.

these early experiences, it was soon realized that exposure to ionizing radiation could be harmful and that protective measures should be taken whenever such radiation is used

Although a general knowledge of the biological effects of ionizing radiation developed rapidly during the early part of this century, research to quantify its effects on living organisms did not begin until the latter half of the 1920's Such research had to await the development of a system of radiation quantities and units, based on rigorous physical principles, with which radiation levels might be accurately recorded.

RADIATION EXPOSURE AND THE ROENTGEN

Steps to develop such a system were initiated by a small international group of scientists shortly after World War I This group proposed the adoption of a unit of *radiation quantity* called the *roentgen* (R), based on the ionization produced by radiation in free air. This unit was defined as the quantity of x- or gamma radiation that produces ions carrying 1 electrostatic unit of either positive or negative charge in 1 cm^3 of air at normal temperature and pressure (i e , 20° C and 1 atm) Soon, international agreement was reached on the specifications of standard ionization chambers and the roentgen was officially adopted as the unit of radiation quantity. To avoid confusion in terminology, radiation quantity was later renamed *radiation exposure*

With the completion of these initial steps to place radiation measurement on a sound footing, research on the biological effects of ionizing radiation began in earnest The first major work was that undertaken by Muller (1927, 1928), who studied the genetic effects of ionizing radiation in fruit flies (work for which he ultimately received the Nobel Prize)

ABSORBED DOSE AND THE RAD

With the growth of radiological methods in medicine and the emergence of nuclear industry after World War II, the system of radiation quantities and units soon required further development It had become apparent that the biological effects of ionizing radiation were related to the quantity of energy absorbed within the exposed tissues and organs Hence, the concept of *absorbed dose,* defined as the mean energy imparted to 1 g of matter, was introduced, and a unit of